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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,277	04/23/2001	Ulrich Feige	A-688A	3317

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,277	FEIGE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7-13,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5, 7-9, 13, 25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/20/2005 has been entered.

Status of Claims

Claims 2-5, 7-13, 25 and 26 are pending in the application

Claims 1, 6 and 14-24 have been cancelled in the response of 1/30/03.

Claims 10-12 have been withdrawn from consideration as being drawn to non-elected invention and species.

Claims 2-5, 7-9, 13, 25 and 26 are under examination.

Specification

Applicants' response on 5/20/2005 to the Office action of 4/22/05 in reference to the Seq. Listing in the specification is acknowledged. Applicants' tabulation of the Seq. listing corresponding to the ones in the specification is gratefully

noted. Applicants' further state that the formulae at page 17, lines 25 and 27 incorporate X-numbered substituents that refer to a defined range of amino acids. The Sequence Listing rules, however, require that each Xaa refer to only one amino acid.

Thus, the only way to comply with the Sequence Listing rules is to provide a separate sequence for each permutation within the formulae. If the Examiner concludes that the permutations within the formulae should not be expressed as sequences within the Sequence Listing, then the Applicants request that the Examiner so state on the record.

In response, while the sequence rules require that each Xaa refer to only one amino acid however, it does not exclude the Markush type of defining the Xaa at specific positions of the sequence. Therefore, it is suggested that applicants define the Xaa at specific location(s) in Markush language for the Xaa substituents.

The amendment filed 5/20/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment page 42, line 26 to page 43, line 6 containing a linker in terms of the Δ symbol. The as-filed

specification does not recite for said symbol in place of a sequence linker. Furthermore, the formulae do not contain a Seq. ID. Nos. The sequence rule requires a Seq. ID. No. for sequences with at least four amino acids in the peptide sequence.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5, 7-9, 13, 25 and 26, as amended are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the last Office action, 1/13/2004.

Response to Arguments

Applicants state that the examiner's argument is styled as a written description rejection. But actually imposes a specific burden of utility beyond that of Section 101. The patent statute only requires that the claimed compounds be useful, not that they avoid degradation. Any active molecule satisfies the utility requirement, whether or not that molecule undergoes degradation. Example 3 of the specification notes that the laminin-5 molecule underwent "some proteolysis" but it also states that "laminin-5 is active", the specification notes that the IC100 was hard to assess accurately due to heterogeneity, but it does indicate that the molecule had activity in the assay. The specification indicates that the degradation products, which maintained the laminin sequence (YIGSR, SEQ ID NO: 7), are active (page 57, lines 11-12). The Examiner is asked to consider that widely marketed pharmaceuticals such as Seldane and Claritine were later found to be pro-drugs having active metabolites. Such molecules were still useful, as demonstrated by their years in use.

In response, the rejection under 112, is not styled as a written description. Rather, is in fact a lack of written description and not lack of utility, as applicants seemed to allude. The degradation of the peptides is but one of the

numerous unpredictable factors that one encounters in this highly unpredictable art. Even for a showing of a single species said degradation has not been foreseen. How much more for a genus of such huge scope containing different adhesion antagonist peptides? Furthermore, heterogeneity of the mixture, as stated above, can also be one of the unpredictable factors that present problems in accurately determining IC value. In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. In order to satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The disclosure of only one species encompassed within a

genus adequately describes a claim directed to that genus only if the disclosure indicates that the applicants have invented species sufficient to constitute the gen[us]. Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004). The more unpredictable the art the greater the showing required (e.g. by (representative examples) for adequate disclosure. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials. University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Applicants, at the time of filing, are deemed to have not invented species sufficient to constitute the genus of sequences of adhesion antagonist peptides and multimers thereof for the recited formula by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004).

Applicants' arguments as to the marketed pharmaceuticals SELDANE and CLARITIN is unclear as to the structural or functional relationship of the marketed pharmaceuticals to the instant claimed composition.

Applicants argue that claim 2 as amended is fully encompassed within claim 12 as originally filed, which required "one or more sequences selected from SEQ ID. Nos. 7 and 9-16." Applicants further argue that one of the priority documents 60/198,919, filed April 21, 2000 was directed toward molecules as claimed in amended claim 2.

In reply, "one or more from the specific sequence Seq. ID. 7 and 9-16" is not a support for the claimed amended of "at least Seq. ID. No. 7". This reads broadly on other sequences than those specifically disclosed as of the filing date i.e., Seq. ID. 9-16. A review of the priority documents does not recite for the amended language "at least Seq. ID. No. 7". Rather a sequence specific to laminin.

Claim 26, as amended, which recites "F1-Δ-YIGSR-Δ-RGD" and "YIGSR- Δ-RGD- Δ-F1" is not supported in the as-filed specification. Applicants in the REMARKS of 5/20/2005, page 3 state that Δ is a linker as contemplated by the inventors.

In reply, the as-filed specification does not refer to a Δ symbol as a linker, which would also read broadly

on any type of linker than those originally disclosed in the as-filed specification. .

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26 as amended, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is unclear as to whether the formula "F1-Δ-YIGSR-Δ-RGD" and "YIGSR- Δ-RGD- Δ-F1" is a part of the claimed composition. It appears to be separate from the claim as the claim ended at line 10 i.e., a period after 1. It is not clear how it is connected to the composition formula of (X1)a-F1-(X2)b.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the

> differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5, 7-9, 13, 25 and 26, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitty et al (US 2002/0155547) in view of Mu (BBRC, Ref. DB) for reasons set forth in the last Office action.

Response to Arguments

Applicants argue that there is no showing why a cytokine as taught by Witty et al would be predictive of success with the laminin pentapeptide. The small size of the laminin pentapeptide alone gives a significant structural difference with interferon beta and other molecules that have been linked to Fc domains. Applicants further argue that there is no suggestion to combine the teachings of the two references except by hindsight reconstruction using the application itself as a guide. It is further argue that the prior art does not predict the results of an improvement in activity from the low micromolar range to the low nanomolar range when coupled to Fc.

In response, the claim composition does not recite a pentapeptide. Rather a composition comprising the pentapeptide i.e., Seq. ID. No. 7. That is, an open-ended language that reads on the whole molecule of laminin. It has been long held that the

use of the term "comprising" leaves a claim open for inclusion of materials or steps other than those recited in the claims". Ex parte Davis, 80 USPQ 448.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As stated in the reply in the last Office action, the combined teachings of the art would have been obvious to one having ordinary skill in the art at the time of filing. Mu teaches that it is obvious to conjugate the YISGR peptides with other carrier besides PEG. Mu discloses that alone, without any carrier, the small size YISGR undergoes degradation (cf. with the disclosure similar findings). It would have been obvious to replace the interferon, which as applicants state, as a cytokine. Mu teaches, or at least suggests, that his findings with cytokine has been presently extended to applyto another, anti-metastatic compound, as the

YISGR containing compounds, cytokines. Furthermore, as taught by Whitty the interferon and, as taught by Mu, can be chemically couple to Ig fusions to any clinically acceptable carrier molecule like polyethylene glycol using conventional coupling techniques. Accordingly, at the time the invention was made, PEG as taught by Whitty and Mu or Fc as taught by Whitty has been used as carrier for different compounds, be it a laminin or its fragments (pentapeptide), interferons or other antimetastic drug. The ultimate goal is similarly achieved, that is to safely deliver the drug, using these carriers, to the intended site without being degraded by proteases.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0812. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
June 24, 2005